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EDITORIAL ARTICLE

Sudden cardiac death: A multidisciplinary approach[☆]

Muerte súbita cardiaca: una aproximación multidisciplinar



Eneko Barbería^{a,b,*}, Youcef Azeli^{c,d}, Alfredo Bardají^{e,f}

^a Institut de Medicina Legal i Ciències Forenses de Catalunya, Tarragona, Spain

^b Departament de Ciències Mèdiques Bàsiques, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, Reus, Tarragona, Spain

^c Sistema d'Emergències Mèdiques de Catalunya, Spain

^d Servicio de Urgencias, Hospital Universitari Sant Joan de Reus, Reus, Tarragona, Spain

^e Servicio de Cardiología, Hospital Universitari Joan XXIII, Tarragona, Spain

^f Departament de Medicina i Cirurgia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, Reus, Tarragona, Spain

Sudden cardiac death (SCD) is a devastating complication of many forms of heart disease.¹ It is a public health problem that may account for 15–20% of all deaths,² with 180,000–250,000 cases annually in the USA.³ One of the main problems in the study of SCD is the difficulty in compiling accurate figures. Reasons for this include the different sources of data used in studies and the lack of consensus on how to define SCD, as we often find that the timing criteria are variable.⁴ Bayés de Luna and Elosúa consider that SCD is likely the most important challenge facing modern cardiology.⁵ Both they and the European Society of Cardiology's SCD working group⁶ define SCD as death occurring unexpectedly within one hour of symptom onset if witnessed, or within 24 h of the person having been observed alive and well if not witnessed.

The *Revista Española de Medicina Legal* (REML) [Spanish Journal of Legal Medicine] has dedicated its entire current issue to the multidisciplinary discussion of SCD, with articles by recognised experts in this field. The issue begins with an article analysing the epidemiology and fatal arrhythmic events that cause SCD,⁷ and includes articles ranging from the *post-mortem* diagnosis of structural pathologies associated with SCD⁸ to the use of now inevitable *post-mortem* genetic analyses.⁹ Also discussed are the important role of toxic substances,¹⁰ the integration of all information into multidisciplinary units studying family history of heart disease (FHD)¹¹ and, lastly, SCD in special circumstances with great social impact.¹²

Bayés de Luna et al. analysed how the incidence of SCD increases gradually and significantly from the third decade of life as a result of coronary artery disease (CAD), the main cause of SCD over the age of 35. CAD is the responsible factor in almost three out of every four cardiac causes of sudden death (SD) in the Eulalia Study, although this proportion is lower compared to Anglo-Saxon countries.¹³ The data that make it possible to compare the incidence of SCD between different countries often come from registers of out-of-hospital cardiac arrest (OHCA). An incidence

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* Corresponding author.

E-mail address: eneko.barberia@xij.gencat.cat (E. Barbería).

has been found in Europe of 38 CPR attempts/100,000 population/year.¹⁴ The first results were recently published from the EuReCa registry (European Registry of Cardiac Arrest), which collects and compares the incidence of OHCA in 27 countries in Europe. In Spain, there were 19 CPR attempts/100,000 population/year, the lowest in Europe.¹⁵ The low incidence is the result of the lower representation coronary heart disease has in overall mortality rates in Mediterranean countries, but may also be explained by multifactorial causes.¹⁶

The authors refer to SCD as the final stage of a chain of events that lead to cardiac arrest, especially resulting from ventricular fibrillation (VF). For each important disorder, they describe the triggers and modulators which, on a vulnerable myocardium, lead to the fatal arrhythmic event responsible for the SCD. They also provide a very illustrative description of the most common arrhythmic events according to the underlying heart disease, highlighting that VF without previous ventricular tachycardia occurs in 70% of acute ischaemic events.

Aguilera-Tapia and Suárez-Mier briefly discuss cardiovascular autopsy, referring to their article published in REML in 2013¹⁷ and to the recently published guidelines of the Association for European Cardiovascular Pathology.¹⁸ They provide excellent iconographic material and begin with the description of the structural heart diseases resulting from atherosclerosis as substrate for CAD. In the sample studied by the authors, atherosclerosis represented 65% of the causes of SD, close to the percentage found in the Eulalia study (58%).¹³ Particularly relevant is the presence of chronic CAD and the relatively low percentage of acute coronary thrombosis (27%) in relation to other series (19–74%).^{2,13} In men, thrombosis is usually associated with atherosclerotic plaque rupture, while in women aged around 50, it is more often the result of plaque erosion. However, above that age, plaque rupture becomes more common with each decade.¹⁹ As the authors point out, coronary thrombosis causes acute myocardial infarction (AMI), although when death occurs early (within 12 h), it does not allow enough time for ischaemic necrosis to become visible in the myocardium. They provide a very practical summary of the timeline of an AMI in the form of a table, which will undoubtedly be of great help in interpreting and explaining the findings to healthcare professionals and relatives, and in court.

Some heart diseases are associated with structurally well-defined abnormalities, but in others the heart is normal. The proportion of autopsies in which no structural cardiac pathology is demonstrated macroscopically varies from 27% to 43% depending on the series, but the proportion decreases after histopathological study.² It is estimated that approximately 50% of SCD cases with negative post-mortem in young individuals are associated with inherited arrhythmia syndromes,² although Campuzano et al. believe the figure is only 30%.⁹ The role of genetic tests on post-mortem samples has emerged from this situation as what is known as *molecular autopsy* or, preferably, post-mortem genetic analysis.¹⁸

Including genetic analyses in post-mortems is recommended by all guidelines in deaths of young people and, according to the European Society of Cardiology's Working Group on the management of patients with ventricular

arrhythmias and the prevention of SCD, it is a Class IIa recommendation.²⁰ These genetic mutations induce abnormalities in the proteins responsible for generating electrical activity in the ion channels of cardiac myocytes, known as channelopathies: long QT syndrome (LQTS), Brugada syndrome (BrS), short QT syndrome (SQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT).⁹ Following an exhaustive study protocol, there is a high probability of diagnosing the cause of SCD,²¹ and the OFRECE study recently found that 0.6–1.1% of the Spanish population aged ≥ 40 has an electrocardiographic pattern showing risk of SD (BrS, SQTS, LQTS).²² This is an important finding as SD is mainly the result of CAD in that age group, and also because in patients with BrS, SD usually occurs in the fourth decade of life.²³ As Campuzano et al. point out, the main challenge now is the genetic interpretation and the clinical translation of the large amount of data obtained in genetic sequencing.⁹

Morentin et al. provide an extraordinary and comprehensive review of the association between SCD and substance use (alcohol, tobacco, cocaine, amphetamines, cannabis, opioids, doping substances and drugs).¹⁰ Beyond the well-known role of smoking as one of the main risk factors for cardiovascular mortality because of its relationship with CAD and acute coronary thrombosis, the relationship between SCD and alcohol, cocaine and cannabis use should be highlighted given the prevalence of their consumption in our environment.

The relationship between alcohol consumption and SCD is not always addressed. It is known that chronic and abusive consumption of alcohol is one of the causes of dilated cardiomyopathy. However, alcohol intoxication can also cause SCD through a proarrhythmogenic mechanism which is still not well understood. The association between recent alcohol ingestion and arrhythmias is known. In 1978, "Holiday Heart Syndrome" was defined by Phil Ettinger as an episode of arrhythmia, most often atrial fibrillation, in a healthy young person with no known heart disease after an episode of excessive alcohol consumption.²⁴

The use of cocaine increases the risk of SCD four-fold,²⁵ so the description of the mechanisms of action that increase the risk of SCD is particularly interesting. It should be noted that the authors represent the two groups to have studied the association between cocaine use and SCD in our environment most extensively, with a prevalence of recent cocaine use in SCD of 7% in Bizkaia²⁵ and 3.1% in Seville.²⁶

The Bizkaia study found the prevalence of cannabis use in SCD to be the same as that of cocaine (7%). There have been numerous studies published to date on the cardiovascular changes caused by cannabis use (increase in heart rate and blood pressure). There is solid evidence that cannabis use is a trigger for acute coronary syndrome and that cardiovascular complications related to cannabis use have higher mortality rates than those not related to cannabis use.²⁷ Given the high prevalence of cannabis use in the Spanish population, we will have to pay close attention to the toxicology results for cardiology emergencies and SCD-related post-mortems in order to monitor how the relationship with cannabis evolves.

Molina et al.¹¹ argue that the forensic autopsy is a key element in the study of FHD and advocate coordination, particularly between health agencies and legal institutions,

through the creation of reference multidisciplinary FHD units. The Unit for Assessment of the Family Risk of Sudden Death in the Autonomous Region of Valencia, which was pioneering in Spain, now has eight years of experience and data, allowing a systematic approach to these cases. The 405 cases of SD protocolised autopsies in patients older than one year and younger than 55 (89% of all cases) confirm CAD as the main cause of death (58%), followed by sudden arrhythmic death (SAD) (23%) and cardiomyopathy (11%). During that same period, the Cardiology Department of Hospital Universitario La Fe studied 500 families (over 2000 family members). They emphasise the legal vacuum that exists in Spain and advocate the creation of an inter-ministerial overall plan, an aspect that would need to be suitably explained, specified and delimited and that first of all would require a study on how these cases are being dealt with in the Autonomous Regions. This is a function in which the traditional role of forensic medicine extends beyond its valuable service to the judicial system and crosses over to health and social care.²⁸ In fact, in the last legislature the Ministry of Justice prepared a draft Royal Decree that would regulate a National SD Registry which was sent to the Forensic Medical Council's Scientific-Technical Committee for study and evaluation.²⁹ We believe it would be worthwhile taking this up again, but this time being more inclusive, with the participation of the Ministry of Health and scientific societies, thus including all the actors involved.

The last article of the monograph refers to SCD in two special circumstances: when associated with practising sport and when it occurs in the context of imprisonment. Pujol and Salas analyse the great variability in the incidence of sudden death in athletes (SDA),¹² although fortunately it is low.³⁰ In the recent retrospective study of OHCA in young people (12–45 years) in the area of Ontario (Canada), 74 OHCA were related to practising competitive and non-competitive sports, implying an incidence of 0.76 cases/100,000 athletes/year.³¹ The authors concluded that sudden cardiac arrest resulting from structural heart disease was uncommon in competitive sports. Nevertheless, the significance of these deaths lies in the fact that many could be prevented by identifying athletes at risk and applying preventive therapeutic measures in appropriate cases. Cardiology tests prior to taking part in sports should therefore be targeted at the early detection of heart diseases involving risk of SD. Although controversial in terms of diagnostic methods, their ability to detect at-risk subjects and their effectiveness in modifying the natural history of these diseases,³⁰ electrocardiogram and echocardiogram would be the most useful investigations for detecting athletes susceptible to SD.³²

However, we must be very careful with the message we transmit to society relating physical activity to risk of SD, given that sport and moderate physical activity are very beneficial for the population's health.

Pujol and Salas also refer to SD in custody. Such deaths can involve significant issues as they occur in the context of a deprivation of liberty, and are attributed to a set of causes such as catecholaminergic discharge when faced with a highly stressful situation (being caught or restrained by the police), usually associated with risk factors (agitated delirium, consumption of stimulant drugs and alcohol, CAD),

which are mutually potentiating³³ and end up causing fatal arrhythmias.

To conclude, several of the authors point out the importance of interdisciplinary work in the approach to SCD, with forensic medicine playing a determining role. Traditionally, the role of forensic medicine has been limited to characterising the causes of SCD, but studies in Bizkaia and the city of Barcelona also indicate that the forensic source should be brought in to improve our understanding of the incidence of SCD.^{34,35} Inclusion of the forensic source of knowledge is known to have a beneficial effect on the statistics for certain causes of death.³⁶ In the case of Catalonia in 2013, this inclusion increased the known mortality rate due to CAD by 5.2%, revealing the under-reporting of the statistics for coronary artery diseases.³⁷

In conclusion, inter-institutional and multidisciplinary collaboration between forensic sources and clinical sources must be promoted. The best example is the creation of SCD registries in which Out-of-hospital Emergency Services also have to be included if our aim is to produce registries of quality,³⁸ and they should finally converge in Multidisciplinary SCD Units, to enable progress in the prevention of one of the biggest challenges in modern medicine.

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